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DEPARTMENT of HEALTH and HUMAN SERVICES

FISCAL YEAR 2001

NATIONAL INSTITUTES OF HEALTH - Volume V
Office of AIDS Research

Justification of Estimates for Appropriations Committees

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Office of AIDS Research

FY 2001 Budget | Page No.

NATIONAL INSTITUTES OF HEALTH

Office of AIDS Research
(INCLUDING TRANSFER OF FUNDS)

For carrying out part D of title XXIII of the Public Health Service Act, $2,111,224,000: Provided, That the Director of the Office of AIDS Research shall transfer funds from this appropriation as authorized by subsection 2353(d) of the Act.

NATIONAL INSTITUTES OF HEALTH

Office of AIDS Research

Amounts Available for Obligation

	1999 Actual	2000 Estimate	2001 Estimate
Appropriation	---	---	$2,111,224,000
Comparative transfer from:			
National Cancer Institute	$234,653,000	$244,494,000	---
National Heart, Lung and Blood Institute	64,511,000	65,527,000	---
National Institute of Dental Craniofacial Research	17,959,000	20,193,000	---
National Institute of Diabetes and Digestive and Kidney Diseases	17,846,000	21,983,000	---
National Institute of Neurological Disorders and Stroke	29,335,000	33,658,000	---
National Institute of Allergy and Infectious Diseases	802,658,000	915,484,000 1/	---
National Institute of General Medical Sciences	31,850,000	37,128,000	---
National Institute of Child Health and Human Development	75,745,000	89,540,000	---
National Eye Institute	10,351,000	10,890,000	---
National Institute of Environmental Health Sciences	7,023,000	7,541,000	---

Amounts Available for Obligation--Continued

	1999 Actual	2000 Estimate	2001 Estimate
National Institute on Aging	$2,068,000	$4,143,000	---
National Institute of Arthritis and Musculoskeletal and Skin Diseases	4,683,000	5,022,000	---
National Institute on Deafness and Other Communication Disorders	1,690,000	1,590,000	---
National Institute of Mental Health	114,105,000	128,697,000	---
National Institute on Drug Abuse	188,919,000	218,227,000	---
National Institute of Alcohol Abuse and Alcoholism	16,187,000	19,243,000	---
National Institute of Nursing Research	6,229,000	7,497,000	---
National Human Genome Research Institute	3,989,000	4,188,000	---
National Center for Research Resources	95,957,000	105,915,000	---
National Center for Complementary and Alternative Medicine	1,030,000	1,030,000	---
John E. Fogarty International Center for Advanced Study in the Health Sciences	12,448,000	14,416,000	---
National Library of Medicine	4,114,000	5,063,000	---
Office of the Director	43,289,000	44,714,000	---
Buildings and Facilities	6,100,000	0	---
Subtotal, adjusted budget authority	$1,792,739,000	$2,006,183,000	$2,111,224,000
Unobligated balance, available start of year	5,665,000	997,000	---
Unobligated balance, available end of year	(997,000)	---	---
Unobligated balance, lapsing	15,000	---	---
Total obligations	1,797,422,000	2,007,180,000	2,111,224,000

JUSTIFICATION
OFFICE OF AIDS RESEARCH

Authorizing Legislation: Sections 301, 2353, and 2356 of the Public Health Service Act, as amended. Reauthorizing legislation will be submitted.

Budget Authority:

FY 1999 Actual	FY 2000 Estimate	FY 2001 Estimate	Increase or Decrease
$1,792,739,000	**$2,006,183,000**	**$2,111,224,000**	**+105,041,000**

INTRODUCTION

The Exploding Global HIV/AIDS Pandemic

Group	People Newly Infected in 1999	People Living with HIV/AIDS	AIDS Deaths in 1999	Total AIDS Deaths
Adults *Women*	5.0 Million *2.3 Million*	32.4 Million *14.8 Million*	2.1 Million *1.1 Million*	12.7 Million *6.2 Million*
Children	570,000	1.2 Million	470,000	3.6 Million
Total ***Source: UNAIDS***	5.6 Million	33.6 Million	2.6 Million	16.3 Million

The potential enormity of the HIV/AIDS pandemic is profound. A recent article in the New England Journal of Medicine stated, "what began as a handful of recognized cases among homosexual men in the United States has become a global pandemic of such proportions that it clearly ranks as one of the most destructive microbial scourges in history. We are at a pivotal point in the evolution of this historic event as we enter the new millennium. ..Unless methods of prevention, with or without a vaccine, are successful, the worst of the global pandemic will occur in the 21st century." HIV has infected more than 50 million people around the world. AIDS already has killed more than 16 million people, surpassing tuberculosis and malaria as the leading infectious cause of death worldwide, according to recent data released by the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the World Health Organization (WHO). This year alone, a record 2.6 million people have died–more than in any prior year. In Africa, for the first time, HIV-infected women aged 15 to 49 outnumber infected men.

The impact on developing nations is staggering, with even greater potential disaster to come. Africa has been the epicenter of HIV/AIDS globally and continues to carry the largest disease

burden, with 70 percent of people living with AIDS worldwide, 83 percent of global AIDS deaths, and 95 percent of the world's AIDS orphans. AIDS has reversed decades of progress from important public health efforts to immunize children, control diseases, and improve nutrition. AIDS is lowering life expectancy and significantly affecting international businesses. If the global spread of HIV/AIDS continues unchecked, South and Southeast Asia, and perhaps China will follow the disastrous course of sub-Saharan Africa. Currently, there are an estimated 6.7 million HIV-infected people in South and Southeast Asia. In India alone, UNAIDS estimates that between 3 and 5 million of its nearly 1 billion population are infected, and the number of new infections is continuing to double every 14 months. Rapid increases also are occurring in Eastern Europe and Central Asia, and AIDS remains a serious threat in Latin America and the Caribbean. HIV infections in the former Soviet Union have doubled in just two years. The Secretary-General of the United Nations has stated that AIDS is having an impact on the gross domestic product in some countries. The micro-economic effects of absenteeism, decline in a skilled workforce, and payments for sickness and death benefits in the developing world will lead to macro-economic effects worldwide.

The coexistence of other endemic diseases widely prevalent in developing countries, such as respiratory and gastrointestinal infections, complicate treatment and pose additional problems for medical personnel caring for HIV-infected individuals. Of particular note is the parallel epidemic of tuberculosis in the developing world. Furthermore, attitudes, beliefs, and taboos surrounding sex; status of women and children; and the source and etiology of AIDS can complicate attempts to control disease transmission and provide appropriate treatment. The contrast in the impact of HIV/AIDS between developed and developing countries is striking, and the factors responsible for this discrepancy, in terms of the diagnosis and care of HIV-infected individuals and the sheer magnitude of the HIV pandemic, are multifactorial.

The HIV/AIDS Epidemic in the United States

In the United States, the epidemic continues to evolve. Although the incidence of new AIDS cases has declined, which is attributed largely to expanded use of new antiretroviral therapies that prevent progression of HIV infection to AIDS, the decline in death rates has leveled off. Further, according to the Centers for Disease Control and Prevention (CDC), the rate of new HIV infections has been constant since 1990 with no decline, meaning that the overall epidemic is continuing to expand. In fact, HIV infection rates are continuing to climb in a number of subpopulation groups, such as women, racial and ethnic minorities, young homosexual men, people over 50 years of age, and individuals with addictive disorders. The recent appearance of multi-drug resistant strains of HIV present a serious public health concern. These data forebode an epidemic of even greater magnitude ahead.

CDC estimates that between 700,000 and 900,000 Americans are currently infected with HIV. Once again, the demographics show that racial and ethnic minorities are more heavily affected. Prevalence of AIDS is higher among African Americans and Hispanics, who account for 45 percent and 20 percent, respectively, of all persons newly diagnosed with AIDS during 1998. CDC's HIV/AIDS Surveillance Report of June 1999 states that among women with AIDS, minorities account for 80% of cases; among men, minorities account for 61% of cases.

NIH AIDS Research Program

In response to this pandemic, the National Institutes of Health (NIH) has developed a comprehensive biomedical and behavioral research program to better understand the basic biology of HIV, develop effective therapies to treat it, and design interventions to prevent new infections from occurring. It is the role of the Office of AIDS Research to plan and coordinate this research program. The changing demographics in the epidemic demand careful consideration in planning our research agenda, since different prevention and intervention strategies must be applied to each subepidemic.

The transmissible nature of HIV makes it radically different from non-transmissible diseases such as heart disease and cancer. The transmissibility of HIV--between individuals and across borders and populations--is what most defines the global pandemic and makes it imperative that the U.S. help address prevention and treatment needs worldwide. The transmissibility of the infection means that there is the potential for unlimited global spread. But it also means that, with the development of appropriate biomedical and behavioral interventions, there is the possibility for dramatic reductions in new infections--and ultimate control of the pandemic--in a way that will never be possible for noninfectious diseases.

By considering the nature of events associated with transmission of HIV and progression of HIV disease, it is possible to identify points of intervention where research can provide the tools needed to reduce transmission and ameliorate the burden of disease. Thus, our intervention research agenda focuses both on prevention of new infections and on treatment of existing HIV infections and clinical AIDS.

Prevention of Transmission

NIH continues to place a high priority on primary prevention of new HIV infections as the most effective means of controlling the spread of the epidemic in the United States and globally. Both behavioral and biomedical efforts are critical to this effort. The OAR is focusing the NIH AIDS research enterprise on intervention research that targets both short- and long-term opportunities to prevent HIV transmission, recognizing that different prevention and intervention strategies must be applied to each subepidemic in the United States and around the world.

Studies have demonstrated that behavioral change can successfully prevent or reduce the spread of HIV/AIDS. Programs resulting from such studies have altered sexual and drug-using behaviors and have reduced the risk of transmission. Yet, a better understanding is needed of how to change the behaviors that lead to HIV transmission—including preventing their initiation—and how to maintain protective behaviors once they are adopted. Biomedical interventions are an important component of a comprehensive primary prevention strategy. The relationship between STDs and increased incidence of HIV infection is well known. Further research into interventions that address this relationship is needed. The vulnerability of women globally to acquiring HIV infection demands the development of effective and acceptable female-controlled barrier methods, such as topical microbicides, to reduce HIV transmission.

Perinatal Transmission

In the United States, regimens of antiretroviral drugs resulting from NIH-supported research have dramatically reduced transmission from infected mother to infant. However, the complexity of

administration and high cost make this option impractical for much of the developing world. NIH-supported clinical trials in Uganda recently demonstrated that a single dose of the non-nucleoside reverse transcriptase inhibitor nevirapine—given to women during labor and followed by a single dose administered to their newborns, at a total cost of approximately $4—reduced transmission by half, compared with a similar and considerably more costly short course of AZT. This advance can substantially lower the cost barrier that has kept many countries from adopting drug strategies that prevent HIV transmission. However, lack of access to other health care services may still affect the ability of developing countries to implement this regimen. Further research on this and other low-cost alternatives is included in this budget request. Another key research issue in this area is the need for a better understanding of the mechanisms involved in HIV transmission through breast-feeding. This is particularly important for developing countries.

Vaccines

There is no question that a safe and effective HIV preventive vaccine is essential for the global control of the AIDS pandemic. In 1997, the President challenged the nation to develop an AIDS vaccine. Consistent with this challenge, NIH funding for HIV vaccine research increased by nearly 100 percent between FY 1995 and FY 2000, resulting in the award of new grants to foster innovative research on HIV vaccines, including vaccine design and development, and the invigoration and reorganization of the NIH vaccine clinical trials effort. Construction of the new intramural Vaccine Research Center began in August 1998 and is expected to be completed by mid-2000. In February 1999, NIH-supported investigators initiated the first AIDS vaccine trial in Africa. The AIDS Vaccine Research Committee, chaired by Nobel laureate Dr. David Baltimore, continues to provide critical advise on all aspects of the NIH AIDS vaccine development program. The changes that have been implemented in this area over the past few years have enormous significance, not only for AIDS but for other diseases as well, as progress made in the development of an AIDS vaccine will have implications for vaccines against other life-threatening illnesses.

Treatment of HIV Infection and AIDS

The development of therapeutics for HIV/AIDS has long been a focus of NIH. Today, many HIV-infected people are living with the benefits resulting from NIH-supported research in this area. The development of protease inhibitors has been extremely successful in extending the length and quality of life for many HIV-infected people in the United States and Western Europe. However, treatment failure now affects a growing proportion of patients receiving therapy. Some patients find it difficult or impossible to comply with arduous treatment regimens, develop toxicities, or cannot afford their high cost of approximately $15,000 per year. Others fail to obtain a satisfactory reduction in viral load even while complying with treatment regimens. In addition, metabolic complications—such as lipodystrophy, hypercholesterolemia, hypertriglyceridemia, hyperinsulinemia, and deforming deposits of abdominal adipose tissue–are beginning to emerge in individuals who have been on long-term antiretroviral regimens that include protease inhibitors. Finally, an increasing number of treatment failures are linked to the increasing emergence of drug-resistant HIV subtypes, which are caused by the extremely rapid rate of virus replication and mutation. The need for simpler, less toxic, and cheaper drugs and drug regimens to treat HIV infection, including new generations of antiviral drugs directed against new targets, continues to be a high priority. Improved regimens are now in clinical trials, and some will be available within the next few years.

Basic and Clinical Science

The development of preventive and therapeutic interventions results from basic biomedical research on the nature of the virus, how it establishes infection, and its mechanisms of pathogenesis, as well as clinical investigations and population-based studies that help to elucidate HIV transmission, disease progression, and the development of sequelae. NIH is conducting studies to provide further information on risk factors and behaviors, identify populations at risk of infection, and describe long-term outcomes of therapies. These studies will provide powerful insights into the prevention and clinical management of HIV disease. Thus, a substantial portion of AIDS-related research will continue to be devoted to fundamental biomedical and behavioral research.

Priority Setting and Development of the FY 2001 Plan and Budget

The Office of AIDS Research has the legislative mandate to develop an annual comprehensive plan and budget for all NIH AIDS research. The plan is distributed widely to the scientific community and is posted on the OAR website. Each NIH Institute and Center (IC) is involved in some HIV/AIDS-related research activity, consistent with its individual mission. The ICs whose research programs are most heavily concerned with HIV, AIDS, and their sequelae are the National Institute of Allergy and Infectious Diseases (NIAID), the National Cancer Institute (NCI), the National Institute on Drug Abuse (NIDA), the National Institute of Mental Health (NIMH), the National Center for Research Resources (NCRR), the National Heart, Lung, and Blood Institute (NHLBI), and the National Institute of Child Health and Human Development (NICHD). The Warren Grant Magnuson Clinical Center provides the infrastructure for intramural clinical studies sponsored by the ICs.

The OAR has established a model for developing a consensus on scientific priorities for the trans-NIH comprehensive research plan utilizing the expertise of both government and non-government scientists as well as representatives of the AIDS-affected community. To foster collaboration and coordination and to participate in the development of the annual plan, the OAR supports six trans-NIH Coordinating Committees in the following research areas: Therapeutics, Etiology and Pathogenesis, Natural History and Epidemiology, Behavioral and Social Science Research, Vaccines, and Information Dissemination. Members of these Committees represent the ICs with the most significant research portfolios in these areas. The Coordinating Committees participate in drafting the Plan for their specific research areas, as well as for training and infrastructure needs in those areas. The plan is then provided to each IC Director and AIDS Coordinator for IC-specific recommendations and input.

To achieve the broadest possible consensus regarding the plan, the OAR then sponsors a series of planning workshops to seek the input of non-NIH experts, including scientists from academia, foundations, and industry as well as AIDS community representatives. These planning groups also include the members of OAR's Prevention Science Working Group; the AIDS Vaccine Research Committee, chaired by Dr. David Baltimore; and the Therapeutics Research Working Group. This year, a new area of special interest section was added to the plan--Racial and Ethnic Minorities. To advise OAR on the scientific priorities in this critical research area, OAR established a new group, the Ad Hoc Working Group on Minority Research. All of these working groups also include AIDS community representatives. These experts, working with the Coordinating Committee members, review and prioritize the objectives and strategies of the plan.

The plan is also reviewed by the OAR Advisory Council. Finally, the planning and budgeting processes are linked, as the plan is provided to the ICs to build their AIDS research budget requests.

The plan serves not only as the framework for the development of the budget, but also for the determination of the use of AIDS-designated dollars, and for tracking and monitoring those expenditures. This budget request is thus framed on the AIDS research areas of the FY 2001 NIH Plan for HIV-Related Research. Key research priorities that would be addressed with new funds are highlighted in each research area.

SCIENCE ADVANCES AND FUTURE RESEARCH DIRECTIONS

THERAPEUTICS

Research Priorities of the FY 2001 Plan

- Develop agents or treatment strategies to destroy or inhibit the expression of HIV in latently infected cells and anatomical and organ reservoirs, therapies for individuals who no longer respond to existing treatments, and new therapeutic regimens that allow for improved compliance and adherence.
- Evaluate the ability of the immune system to maintain or repair itself after viral suppression has been achieved through HAART; evaluate cytokines, modulators, and other immunoactive agents to prevent further immune deterioration and to reconstitute deficient immune systems in HIV-infected individuals; and evaluate immunotherapeutic approaches to increase immune responses following antiretroviral therapy.
- Develop agents targeted at drug-resistant HIV strains.
- Support the discovery and development of improved, acceptable, effective, and safe physical and chemical barrier methods—including topical microbicides and other methods—to reduce sexual transmission of HIV and sexually transmitted diseases (STDs) in developed and developing nations.

Ground breaking research in basic biology has led to a revolution in drug design and diagnostic methodologies that are benefitting the fight not only against AIDS, but also against other diseases. This basic research has been the foundation for the development of medications that are extending the length and quality of life for many HIV-infected individuals. Additional research, however, is needed to maximize the likelihood of continued success in treating HIV-infected individuals with these multidrug combinations. The most compelling questions in this area include the following:

- How long can the virologic, cellular, and clinical responses be maintained on an initially successful regimen?

- What are the earliest detectable signs of failure that indicate that the drug regimen should be changed?
- What are the most common reasons for failure of these regimens?
- Can treatment strategies aimed at minimizing the risk of clinical progression be developed?

***Story of Discovery*:**

HIV Infection Persists Even With Combination Drug Therapy

HIV infection can be controlled with combination drug treatments which delay disease progression and prolong survival. Mathematical modeling of virus levels had predicted that two or more years of combination therapy might completely eliminate HIV from the body, however more recent reports suggest that a reservoir of viable HIV may persist in some cells, which would necessitate indefinite continuation of combination therapy to keep the virus in check.

Scientists at Northwestern University Medical School used sensitive indicators of viral activity to test blood samples from HIV-infected patients who were undergoing combination therapy and who had previously undetectable levels of HIV in their blood for 20 months or more. The sensitive tests confirmed the presence of persistent reservoirs of viable HIV, even after two or more years of combination therapy. The persistence of this infected cell population and incomplete suppression of viral replication -- not previously predicted by mathematical models -- mean that mathematical predictions of viral eradication are not yet reliable.

Combination drug treatments are complex, expensive, and difficult for patients; however, it was hoped that the therapies would eventually eliminate the HIV from the body. The current study indicates that HIV may not be eradicated with current treatments; therefore, improved models of HIV infection and new treatments must continue to be pursued. More effective and less toxic long-term medications are critically needed to suppress HIV replication.

Currently available antiretroviral drugs are not able to achieve complete viral suppression. HIV continues to replicate at low levels in various reservoirs or sanctuary sites, making it possible for drug-resistant strains to emerge. Recent research has demonstrated the existence of a reservoir of latently infected cells that persists for prolonged periods of time, even in patients whose plasma viral load decreases to undetectable levels. These cells are infected during the acute phase of primary infection and form a source for HIV replication following drug withdrawal or HIV gene activation. Research is needed to develop new drugs that are safe and effective, can penetrate all compartments of the body, can be easily adhered to, and possess few toxic or complicating side effects, such as metabolic complications and body composition alterations, which have been associated with protease inhibitors. Given the limits of current antiretroviral therapies, immune-based and immune restorative therapies are needed, especially for individuals at more advanced stages of disease and immune depletion.

The evaluation of potential therapies for the treatment of HIV infection and its associated opportunistic infections (OIs), malignancies, and other complications is one of the highest priorities. Antiretroviral and OI prophylaxis regimens are becoming increasingly complex with respect to drug-drug interactions and adherence. Protease inhibitors, in particular, interact with

each other and many other medications commonly used by HIV-infected individuals. Additional research is under way and planned to address these issues with the goal of minimizing viral replication and delaying disease progression and development of HIV-related manifestations, including metabolic complications and body composition transformations.

ETIOLOGY AND PATHOGENESIS

Research Priorities of the FY 2001 Plan

- Capitalize on new insights into HIV biology and HIV host interactions to identify new viral and cellular targets for therapeutics, microbicides, and vaccine development.
- Investigate the mechanisms of HIV persistence in the setting of effective antiretroviral therapies.
- Elucidate direct and indirect mechanisms of T-cell depletion and reconstitution in HIV infection and in response to therapy.
- Improve our understanding of the mechanisms underlying metabolic abnormalities and body composition changes during HIV infection and following effective antiretroviral therapies, and determine the risk of atherosclerotic cardiovascular disease in these settings.

To ensure the continued growth of a powerful arsenal against HIV, it is imperative that scientists continue to study HIV pathogenesis and identify new targets for the design of drugs and vaccines. Design and development of new drugs are based on the study of the fundamental structural properties of the relevant viral targets. The foundation of rational drug design emerged, in large part, from basic research supported by NIH and the pharmaceutical industry over a number of years. Although the potential benefits of this approach to drug development have yet to be fully realized, it will have increasing applications to all aspects of human health and disease. Efforts to develop effective therapies to treat HIV infection and its associated illnesses are providing a critical proving ground for the concept of rational drug design and for the refinement and advancement of its methods.

Basic research plays a vital role in the development of interventions to block transmission and slow disease progression in all populations at risk. The research programs of the NIH will continue to support a broad and vigorous program to study life processes, using cutting edge methods. This area of investigation, driven by investigator-initiated research, has provided the constantly advancing knowledge base that permits the development of new applications for the prevention and treatment of disease.

The challenge of understanding HIV infection and disease also represents an extraordinary example of how the biology of other infectious diseases may be studied in the future. Never before has the behavior of an infectious microorganism within an infected human been examined in such detail. For this type of investigation, new research tools are required to facilitate sensitive, high-resolution analyses. The amount of virus present in an infected person must be

determined and its level of replication and consequent damage measured. The need to understand HIV infection has driven technological developments in this area, and much of this effort has been fueled by support provided by NIH.

The powerful tools developed to monitor the location and extent of HIV replication within infected persons have elucidated critically important details of how HIV infection leads to AIDS. Application of these new tools has revolutionized our understanding of the extent of HIV replication that takes place in infected people and how virus replication is directly linked to the destruction of T cells and the resultant compromise of the immune system. The broad outlines of the pathogenic mechanisms of HIV disease are now known, but the precise details of the process await definition. An improved understanding of these issues is necessary to permit definition of the optimal ways to use therapies to treat the primary HIV infection and its associated opportunistic complications. The recently developed genotypic and phenotypic assays will permit further characterization of the unique drug sensitive/drug resistant strains of HIV. These assays will allow the development of more effective and individualized therapeutic regimens to increase patient longevity, delay disease progression, and improve quality of life.

Insulin resistance, hypercholesterolemia, hypertriglyceridemia, and abnormal fat distribution (either depletion or accumulation) have been described in HIV-infected individuals taking antiretroviral therapies. These manifestations are a serious cause of concern with broad public health implications. Patients are experiencing problems in adhering to regimens when these symptoms occur, some stop taking medications, and others are not initiating therapies due to the possible occurrence of disfiguring physical changes and long-term cardiovascular complications. Elucidation of the factors contributing to metabolic abnormalities and body composition changes will allow effective therapies to be tailored to the specific mechanism by which they occur, with the potential for enhancing quality of life in HIV-infected persons. Although the incidence of wasting has declined, wasting remains one of the most devastating aspects and one of the major causes of morbidity and mortality in individuals who do not respond or lack access to potent antiretroviral therapies. Weight loss in AIDS results in a significant reduction in survival, independent of other factors influencing survival, including CD4 cell count and history of infection or malignancy.

AIDS is associated with a broad spectrum of cancers and tumors, including Kaposi's sarcoma (KS), lymphomas, human papillomavirus (HPV)-related cervical and anogenital carcinomas, and hepatitis B-related hepatocellular carcinomas. Because HIV causes immunosuppression and most AIDS-associated malignancies are strongly associated with viruses, HIV infection provides a unique model to study the interplay of viruses, a dysfunctional immune system, and the development of cancers. Elucidation of the interactive factors involved in the pathogenesis of AIDS-associated malignancies will possibly translate in the identification of new targets for prevention and treatment.

HIV infection results in progressive damage of the immune systems of infected individuals and makes them susceptible to a diverse collection of bacteria, viruses, fungi, and protozoa that represent the major causes of suffering and death for HIV-infected individuals. Opportunistic infections can affect virtually every tissue and organ system in the body, resulting in severe

functional compromise. NIH currently supports a comprehensive portfolio of basic research on the pathogenesis of AIDS-associated OIs.

SCIENCE ADVANCE:
gp41 BLOCKERS RAISE HOPE FOR NEW CLASS OF ANTI-AIDS DRUGS
In 1997, NIH-supported scientists determined the detailed, three-dimensional structure of a glycoprotein called gp41, a protein responsible for the HIV infectivity. The structure revealed an attractive drug target–a deep pocket that, if blocked, would likely shut down gp41 and thwart HIV infection. This year, two groups of researchers used this structure to rationally design molecules that block the action of gp41. These molecules may serve as precursors for entirely new anti-AIDS drugs. One of the groups took advantage of the fact that normal proteins exist in only one conformation, as if they were all "right handed." This group designed small protein mimics that are "left-handed." Several of these molecules bind to gp41 and, in test-tube experiments, block HIV infectivity. Because the molecules are unnatural, left-handed compounds, they do not trigger an immune response and are less susceptible to attack by the body's natural degradative enzymes. They are also small enough to be delivered orally, in contrast to T-20, a peptide that targets gp41 and is in Phase II clinical trials. Using sophisticated technology, another investigator has recently generated tens of thousands of small organic molecules that may prevent HIV infection. Both of these reports provide hope that we may have a new class of drugs in the anti-HIV arsenal.

NATURAL HISTORY AND EPIDEMIOLOGY

Research Priorities of the FY 2001 Plan

- Conduct studies on primary early infection and its impact on HIV transmission.
- Develop and maintain the domestic and international infrastructure for epidemiology cohorts and prevention studies.
- Conduct prevalence and natural history studies on HIV-1 clades and HIV-2 to provide a better understanding of how the host controls the virus—including studies of viral acquisition, pathogenesis, and disease progression—and determine the correlates of immunity associated with long-term survival.
- Investigate, through epidemiology studies, the short-term, intermediate, and long-term effects of antiretroviral therapy usage during pregnancy and the postpartum period on the mother, fetus, and newborn.

Epidemiologic research continues to show the demographics of HIV infection and AIDS in the United States shifting from an illness primarily affecting homosexual and bisexual men to an epidemic with increasing and disproportionate rates of infection in minorities, women, adolescents, drug users, and heterosexuals. This shift has placed urban, minority and disenfranchised communities at the intersection of several overlapping epidemics: AIDS, STDs, TB, and drug use. NIH supports studies to examine the transmission of HIV, the progression of HIV-related disease (including the occurrence of OIs), the development of malignancies, the

incidence of neurological and neurobehavioral dysfunction, the occurrence of oral manifestations, and the development of other sequelae. Such studies examine the effects of viral factors, host factors, and other factors on the risk of infection and disease progression, which will provide useful insights into the prevention, as well as management of HIV infection.

International epidemiologic studies supported by NIH contribute significantly to the understanding of the cellular and molecular mechanisms of HIV transmission, the progression of HIV-related disease, and the risk factors associated with HIV infection. These studies also contribute to the development of new biomedical and preventive behavioral intervention strategies. NIH-sponsored natural history and epidemiology studies are investigating the transmissibility of non-B HIV clades and the reduction of HIV transmission through prevention and treatment of coexisting STDs as a means of primary HIV prevention.

Another area of primary prevention research focuses on developing new or improved means of reducing perinatal transmission in the United States and worldwide, with particular emphasis on methods appropriate to the developing world. NIH is supporting studies to better understand the timing, mechanisms, and risk factors of perinatal transmission; whether specific strains are more likely transmitted; the potential benefit of Caesarean section; and development of newer therapeutic regimens and immunotherapy. The virtual elimination of perinatal transmission in our nation and the world is a goal that is being vigorously pursued.

Ethnic and racially diverse cohorts of HIV-infected individuals and HIV-uninfected individuals at risk of infection are followed in clinical epidemiology studies at domestic and international sites. By maintaining this diversity, data obtained from such studies will have validity for all communities impacted by HIV infection.

NIH is supporting studies on the occurrence, natural history, and molecular epidemiology of HIV-associated preneoplastic conditions and cancers. These efforts are designed to address the significantly increased incidence and aggressiveness of cancers and preneoplastic conditions in immunodeficient individuals; e.g., increases in cancers associated with oncogenic human viruses such as non-Hodgkin's lymphoma, Hodgkin's lymphomas, Kaposi's sarcoma (KS), and human papillomavirus. Recent data continue to implicate HHV-8 in the development of KS, some non-Hodgkin's lymphomas, and multiple myeloma. Ongoing efforts are being focused to better understand the natural history and epidemiology of HHV-8. The importance of this and related research will increase further as the incidence of AIDS-associated malignancies are expected to increase as the life expectancy of HIV-infected patients is extended with combination therapies and prophylaxis for HIV-related opportunistic infections.

NIH will continue to place a priority on natural history studies on the unique clinical manifestations and nature and rate of disease progression in women, the impact of HIV on cervical cancer, the effects of HIV and human papillomavirus (HPV) coinfection, and the development of an HPV vaccine for control of cervical cancers. NIH is also pursuing studies of HIV-related gynecological complications, e.g., cervical dysplasia, pelvic inflammatory disease, *Candida* vulvovaginitis, and genital ulcers associated with HIV and other STDs.

BEHAVIORAL AND SOCIAL SCIENCES (including Non-Vaccine Prevention)

Research Priorities of the FY 2001 Plan

- Better understand and address through interventions the psychological, social, economic, and cultural dynamics of gender and sexual identity that operate in HIV risk, protection, and care.
- Develop and test interventions among individuals living with HIV/AIDS and other comorbid conditions (e.g., substance abuse, mental illness, hepatitis, tuberculosis, homelessness).
- Identify and address issues in the initiation, maintenance, sustainability, and durability of effective HIV prevention and care efforts among individuals (including HIV-infected individuals) and communities over time.
- Improve translation and transportability of effective HIV prevention and care interventions, domestically and internationally.

The primary goal of NIH-sponsored AIDS-related behavioral and social science research is to discover how to change the behaviors that lead to HIV transmission—including preventing their initiation—and how to maintain protective behaviors once they are adopted. An additional goal is to reduce the negative impact of HIV on individuals with HIV infection, their families, the health care system, and society.

NIH sponsors research related to the following: developing, implementing, and evaluating behavioral and social interventions to reduce HIV transmission in a range of populations and settings; strengthening our understanding of the determinants, trends, and processes of HIV-related risk behaviors and the consequences of HIV infection; developing and evaluating behavioral strategies for preventing or ameliorating the negative physical, psychological, and social consequences of HIV infection; and improving the research methodologies employed in behavioral and social science research.

It is imperative to better understand the behaviors that influence HIV transmission and protection and to develop and implement prevention programs based on this understanding. Scientifically-based interventions have been demonstrated to alter sexual and drug using behavior and reduce the risk of transmission among a number of population groups, but we are still far from realizing the full potential of such prevention research on a global scale. A more refined understanding of social and cultural factors that contribute to HIV risk or protection, particularly in minority communities, will have an enormous influence on the successful implementation of a broader range of preventive or therapeutic measures. Drug users and their sex partners are the fastest growing segment of AIDS cases in the United States and in many other countries. High priority is being given to research to understand the phenomenon of addiction itself, as well as the complex interaction of alcohol use, drug use, and poor impulse control, and to develop effective interventions from that knowledge base.

The development of new and more effective drug therapies—in particular combination therapies—for combating HIV infection has raised a host of behavioral questions that have significant implications for HIV prevention and treatment. With combination therapies, the number of drugs and frequency of dosing require strict adherence to regimens that may be difficult for many people to achieve. Lack of complete adherence may result in the development of drug-resistant strains of HIV, which could have devastating implications for our ability to stem transmission and treat HIV-infected individuals. In addition, as HIV-infected individuals experience improved health and a decline in detectable virus in their body as a result of taking the new combination therapies, they may believe that they are less infectious and may lapse into unsafe sexual and drug-using behaviors. This could have the effect of increasing HIV transmission, if the virus is still viable at undetectable levels. These issues highlight the importance of research on how best to ensure adherence to both pharmacological and behavioral HIV-related interventions.

VACCINES

Research Priorities of the FY 2001 Plan

- Develop and test new vaccine strategies, alone or in combination, to induce broad functional immune responses—both humoral and cellular, mucosal and systemic—against HIV isolates from all genetic clades.
- Continue to improve animal models and to improve availability of nonhuman primate models for systematic, comparative efficacy testing of vaccine concepts and understanding of the mechanisms of protection that might be translated to HIV vaccine studies in humans.
  - Develop MHC-defined and/or histocompatible rhesus macaques, and define the associated epitopes of HIV/SIV proteins for vaccine studies.
  - Continue to develop and exploit SHIV chimeric viruses with different degrees of virulence to more closely reflect disease progression observed in HIV-infected people and the genetic variation observed in worldwide HIV epidemics.
- Enable rapid movement of vaccine concepts into clinical testing, including the development or procurement of GLP/GMP products or direct funding for production of candidate vaccines to stimulate industry partnerships for human and nonhuman primate trials.

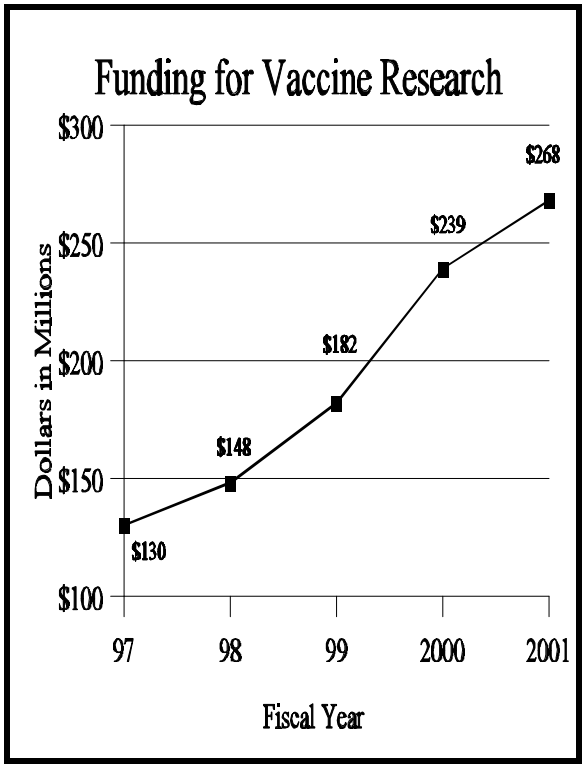
Vaccine research remains one of the highest research priorities. The toll of the epidemic in poorer countries where therapeutic and prevention interventions are unavailable or unaffordable, as well as in industrialized parts of the world, dictates the important emphasis on vaccine development. A safe and effective vaccine is the critical missing element in our armamentarium for the prevention of HIV and ultimate control of the pandemic.

To address the scientific obstacles and facilitate AIDS vaccine development, NIH continues to increase support for a broad program encompassing basic, preclinical, and clinical vaccine research on candidate vaccine products. As promising vaccines move further in the vaccine pipeline, expanded trials with populations at higher risk for HIV infection will become increasingly important. HIV/AIDS vaccine research requires trained health care, medical research, and prevention specialists from the populations at risk who will be integrally involved in development of vaccine candidates and clinical vaccine and prevention trials. International and domestic trial sites are being developed, including a cadre of trained indigenous or minority personnel, to conduct vaccine trials with the direct involvement of the communities at risk.

The development of an AIDS vaccine is a complex research challenge because HIV is unusually well-equipped to elude immune defenses, as exemplified by its ability to persist in almost all instances and eventually overcome the immune system. Many different vaccine approaches are being pursued. Initial studies are leading to more advanced vaccine candidates that may provide protection.

SCIENCE ADVANCE:

PROGRESS TOWARD DEVELOPMENT OF AN HIV/AIDS VACCINE



Vaccine researchers face a number of significant challenges, including the variability of HIV– the existence of multiple strains of the virus, coupled with the high frequency of genetic mutation characteristic of HIV. Because of this variability, design of a broadly effective vaccine is especially desirable. Researchers developed HIV vaccine immunogens (molecules capable of eliciting an immune response) that incorporate portions of specific HIV surface proteins that are exposed transiently during the process of binding and fusion of the virus with a target cell. Blood from mice injected with these immunogens was able to neutralize 23 of 24 different HIV strains. Researchers hypothesize that this broad effect may be elicited because some region in the fusion-competent immunogen is so fundamental to HIV function that it does not mutate across HIV strains. This is a major advance because it constitutes the broadest immune response elicited against HIV by a single immunogen to date. Although the findings are preliminary, the demonstration that a single HIV immunogen can neutralize multiple HIV strains provides hope that the development of a broadly protective vaccine is possible.

Clearly, it will be more difficult to formulate an HIV/AIDS vaccine than was the case for prior vaccines directed against acute viral diseases. The scientific community must be mustered to make a broad and diverse attack upon this daunting challenge. Vaccine research is needed to attempt to unravel a wide variety of questions about the structure of the virus, its immunogenicity, the protective role of different components of the immune response, and the mechanism of viral escape from immune surveillance. In addition, fundamental work must be done to develop and refine a number of potentially effective methods for presentation of HIV antigens, including vectors engineered from a wide variety of viruses, and naked DNA itself. Building on this base, it will probably be important to utilize primate models to elucidate the mechanisms of protective immunity and to screen a multitude of candidate immunogens for the most promising products for clinical trials in humans.

RACIAL AND ETHNIC MINORITIES

Research Priorities of the FY 2001 Plan

- Develop, test, evaluate, and disseminate culturally sensitive and appropriate prevention interventions in racial and ethnic minority communities to reduce HIV transmission and acquisition in at-risk social networks. To the maximum extent possible, these interventions should intersect at multiple levels and reflect the role of socioeconomic status and language.
- Identify and address gaps in care, treatment, and research manifested by the differentials in access to care and HIV-associated morbidity and mortality in majority and minority HIV-infected communities.
- Identify, define, and address the infrastructural, technical, methodological, and sociocultural needs of communities of color for clinical trial participation.
- Support and expand programs that train racial and ethnic minority investigators in the areas of behavioral and social science, clinical research, and basic science to increase the number of investigators trained and funded to successfully complete such research.

NIH supports biomedical and behavioral research aimed at preventing, treating, and controlling HIV infection and its sequelae in minority communities. This year, OAR added a new section of the strategic plan to address research for racial and ethnic minorities. The disproportionate impact of the ongoing HIV/AIDS epidemic upon communities of color has presented significant challenges to biomedical, behavioral, social, and clinical research. The multifaceted nature of the epidemic in general, and specifically within racial and ethnic minority communities, requires a range of research interventions that target those components of the epidemic that facilitate, as well as limit, transmission. Within these communities, the impact of the main routes of HIV transmission in the United States—unprotected sexual intercourse and injecting drug use—are further confounded by other societal and community factors. These factors include poverty, homelessness, immigration, racism, violence, religion, social stigma, the sociocultural roles of women, the impact of acculturation, and homophobia.

NIH has for many years taken strong steps to assure minority participation in clinical trials, natural history and epidemiologic cohorts, and in prevention studies and to assure that the overall research agenda is responsive to the needs of minority communities. Minority participation in clinical trials must continue to keep pace with minority representation in the epidemic. For such participation to occur, research to identify the barriers to participation in clinical trials, as well as provider- and client-related barriers and needs, is essential.

NIH supports a broad array of behavioral intervention studies with specific focus on African American populations. These studies are characterizing the disease process in drug users, factors influencing disease progression, consequences of multiple co-infections, effectiveness of therapeutic regimens, and impact of health care access and adherence to therapeutic regimens on disease outcomes. The rising numbers of minority AIDS cases provide a powerful reminder that behavioral research must continue to define and utilize cultural, social, and contextual factors that affect HIV risk behavior. The role of alcohol and drug use in facilitating HIV transmission through social networks in all communities must also be explored within these social frameworks.

NIH has established programs and policies specifically designed to recruit individuals from underrepresented racial and ethnic groups into research careers and to build research infrastructure in minority institutions. These programs provide training and research opportunities across the continuum from high school students to independent investigators. NIH also supports activities with the goal of disseminating research information to health care providers serving minority communities as well as directly to individuals at risk.

OTHER AREAS OF INTEREST

International AIDS Research

The exploding nature of the epidemic globally, particularly in the poorest parts of the world, has escalated the urgency of improved intervention strategies. For this reason, NIH will significantly increase its investments in international studies in the coming year. NIH supports a growing portfolio of research conducted in collaboration with investigators in developing countries. Results of this research benefit the people in the country where the research is conducted as well as people affected by HIV/AIDS worldwide. In addition, NIH supports an active program for training of researchers and health professionals from many countries.

For example, NIH collaborates with UNAIDS, host country governments, and in-country scientists in vaccine development and preparation for efficacy trials. Sites have been established in Uganda, South Africa, Haiti, Malawi, Thailand, India, Zimbabwe, Zambia, Trinidad and Tobago, Brazil, and Kenya. NIH-sponsored programs target studies on factors related to transmission of HIV and the pathogenic mechanisms associated with HIV disease progression through a number of studies in Africa, Asia, and Latin America. These studies focus on the biologic determinants of infectiousness and susceptibility.

It is critical to the success of international studies that foreign scientists be full and equal partners in the design and conduct of collaborative studies and that they have full responsibility for the

conduct of studies in-country. To that end, the NIH supports international training programs and initiatives that help to build infrastructure and laboratory capacity in developing countries where the research is conducted.

In recognition of the critical need to enhance NIH international research efforts, the OAR has established the NIH International AIDS Research Collaborating Committee. The Collaborating Committee provides a forum for discussion of current and planned international HIV research efforts of the NIH, other government agencies and departments, and international organizations; discussion of key scientific policy and bioethics issues in international research; and exchange of scientific information. The group includes representatives of the NIH institutes with major international AIDS research portfolios as well as other agencies, departments, and international organizations, including DHHS Office of International Affairs; DHHS Office of HIV/AIDS Policy, the Centers for Disease Control and Prevention (CDC), Food and Drug Administration (FDA), Department of Defense (DOD), U.S. Census Bureau, National Security Council, White House Office of National AIDS Policy, World Bank, and U.S. Agency for International Development (USAID).

Training and Infrastructure

The NIH will continue to support training of domestic and international biomedical and behavioral AIDS researchers as well as the improvement of facilities and equipment for the conduct of AIDS research, including support of animal facilities for animal model research. Numerous NIH-funded programs have increased the number of training positions for AIDS-related research, including programs specifically designed to recruit individuals from minority communities into research careers and to build research infrastructure in minority institutions. The NIH Loan Repayment Program (LRP) was mandated by Congress under Public Law 100-607 in 1988 and authorized under 42 USC 288-1 to encourage health professionals to engage in AIDS-related research at the NIH. The Fogarty International Center sponsors the AIDS International Training and Research Program (AITRP), a program established in 1988 at the request of Congress to train scientists in developing countries to undertake AIDS research. The goal of the program is to expand scientific capabilities in the epidemiology, prevention, diagnosis, and treatment of HIV/AIDS throughout the world and to facilitate the evaluation internationally of AIDS interventions, such as vaccines and other strategies. The Regional Primate Research Centers (RPRC) Program, supported by the National Center for Research Resources, provides specialized facilities, scientific and technical personnel, animal models research and breeding, and a wide variety of non-human primate species to support diverse requirements for AIDS-related research.

Information Dissemination

Effective information dissemination approaches will continue to be integral to HIV prevention and treatment efforts. Such programs are critical in light of the continuing advent of new and complex antiretroviral treatment regimens, the adherence issues related to HIV/AIDS treatment, the need for research communities to work and communicate globally, and the need to translate behavioral and social prevention approaches into practice. The changing pandemic and the increasing number of HIV infections in specific population groups, such as minorities and women, also underscore the need to disseminate HIV research findings and other related information to communities at risk. The flow of information among researchers, health care

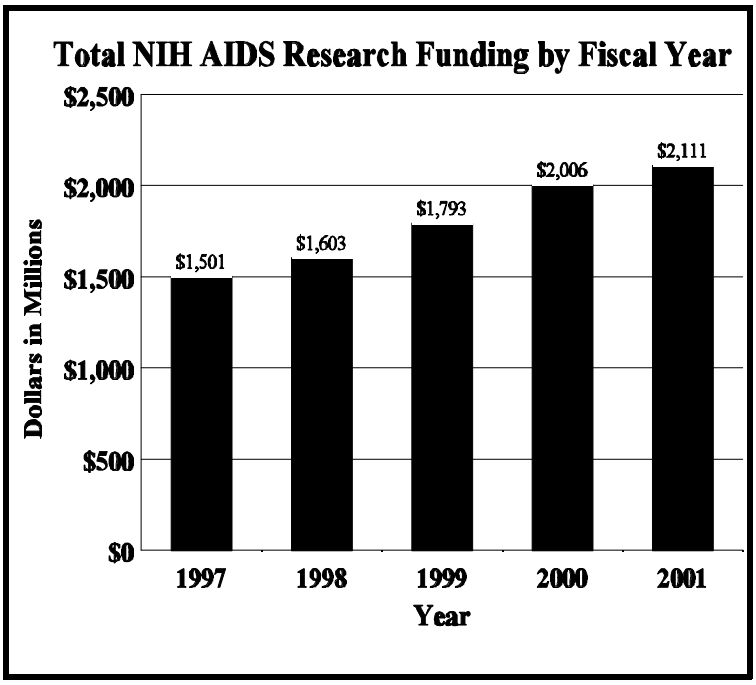
providers, and the affected communities represents new opportunities to rapidly translate research into practice and to shape future research directions.

AIDS Research Benefits Other Diseases

The investment in AIDS research has provided a new paradigm for confronting viral diseases in general. Prior to the development of these potent drugs, virtually all efforts to deal with viral diseases involved prevention (using vaccines) or palliation (treating symptoms). Few effective treatments were available for most common viral infections. The investment in AIDS drug development has already had an impact on the treatment of hepatitis B infection. The drug lamivudine (also known as 3TC), initially developed to treat HIV infection, now has been shown to be a highly effective inhibitor of hepatitis B virus replication and is being used to treat chronic hepatitis B infection. The advanced technologies and skills used in developing protease inhibitors for HIV are now being applied in the discovery and development of new agents against hepatitis C virus. Using these techniques, new candidate drugs have been designed to treat cytomegalovirus (CMV) infection.

AIDS research has enormously enhanced our understanding of the human immune system. Among the important diseases that may benefit from this research are multiple sclerosis, juvenile diabetes, rheumatoid arthritis and systemic lupus erythematosus. Effective drug regimens developed to both prevent and treat many of the microorganisms that cause opportunistic infections in AIDS patients also provide real benefit to patients undergoing cancer chemotherapy or receiving anti-transplant rejection therapy. AIDS research also has led to a better understanding of the mechanisms through which the blood/brain barrier functions. This knowledge has important implications for research on Alzheimer's disease, dementia, multiple sclerosis, neuropsychological disorders, encephalitis, and meningitis.

Rationale for the Budget Request



The President's budget request for the NIH Office of AIDS Research–which includes all AIDS funding for the Institutes and Centers of the NIH–is $2,111,224,000, a 5.2 percent increase over the comparable FY 2000 Estimate of $2,006,183,000. The FY 2001 funding level for the Office of AIDS Research will provide the necessary continued support for all areas of AIDS research, especially the priority areas of vaccine research, therapeutic research, and behavioral and prevention science research as set forth in the NIH FY 2001 Plan for HIV-Related Research. These priorities were determined by the OAR Director with the support of the Office of AIDS Research Advisory Council. A five year history of NIH AIDS funding levels for the OAR are shown in the graph above.

This budget request will allow for increased efforts, including important new research initiatives, to develop new AIDS vaccine candidates and to advance these candidates into pre-clinical testing in animal models and clinical trials as soon as possible. The FY 2001 funds also will permit an increased emphasis on prevention science research, including the development and evaluation of interventions to prevent infection, such as microbicides and other female-controlled barriers, as well as new behavioral strategies to prevent HIV transmission. This budget provides substantial funds to support the discovery and development of more effective, less toxic, less complicated, less expensive therapeutic regimens for the treatment and control of HIV infection and its complications. This budget will also address critical strategies to prevent HIV transmission among racial and ethnic minority populations where the disease is now taking a disproportionate toll.

Budget Policy

The Office of AIDS Research continues to emphasize investigator-initiated research, as demonstrated by the chart on the next page showing that research project grants (RPGs) constitute 59 percent of the NIH AIDS budget. This represents a 4 percent increase for RPGs over the FY 2000 level. This emphasis on RPGs allows NIH to support new scientific opportunities in AIDS research.

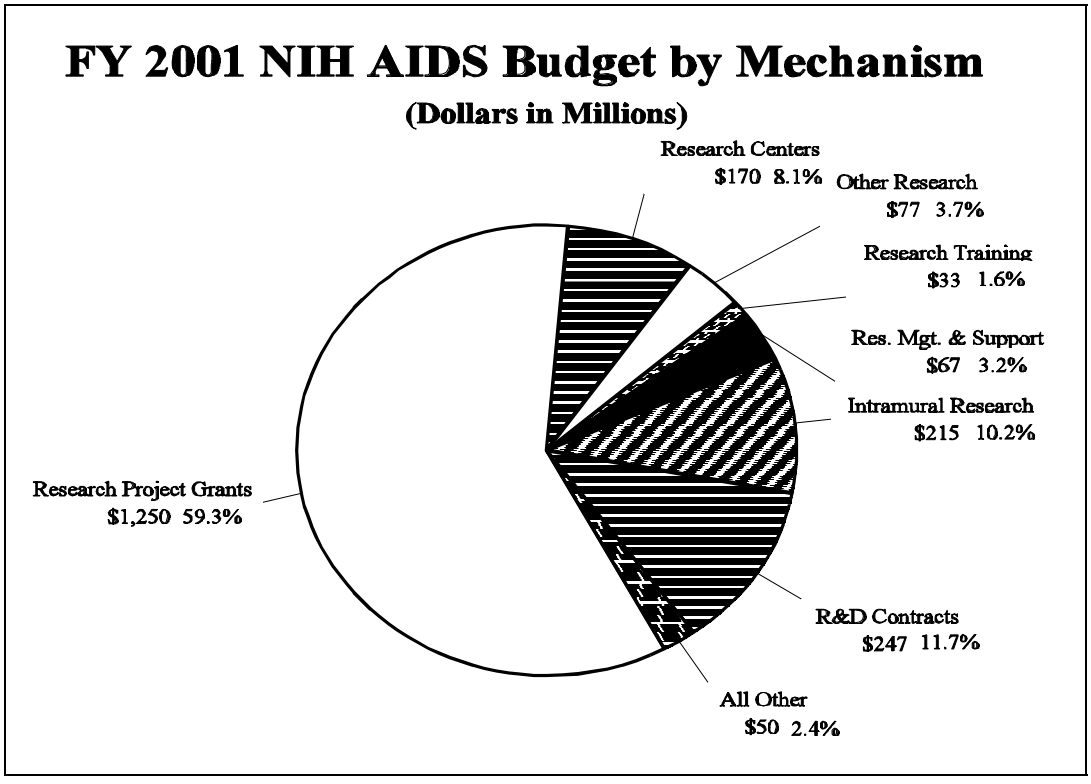
To control the growth of continuing commitments and support planned new and expanded initiatives, the Fiscal Year 2001 request provides average cost increases of 2 percent over Fiscal Year 2000 for competing research project grants. Noncompeting research project grants will receive increases of 2 percent on average for recurring costs. This strategy will ensure that NIH can maintain a critical number of new awards, especially for new researchers.

The FY 2001 request includes funding for a total of 51 research centers–the same number supported in FY 2000. These centers play a crucial role in enhancing the research activities of investigator-initiated research.

The FY 2001 request also includes 269 "other research" grants, including 198 career awards, an increase of 10 grants over FY 2000. Research and development contracts will total 192 in FY 2001–an increase of 6 contracts over FY 2000. This increase in research and development contracts represents funding for the new HIV Prevention Trials Network, the new HIV Vaccine Trials Network, and the Simian Immunodeficiency Virus Vaccine Evaluation Unit.

Training continues to represent an important component of the AIDS research program. The nature of AIDS research requires multi-disciplinary training. There is a continuing need for new investigators in AIDS research, and this budget request supports additional training opportunities. In the Fiscal Year 2001 request, the OAR will support 856 pre- and postdoctoral trainees in full-time training positions. Stipends will increase by 2.2 percent over FY 2000 levels.

The mechanism distribution by dollars is displayed below:



NATIONAL INSTITUTES OF HEALTH

OFFICE OF AIDS RESEARCH

SUMMARY BY MECHANISM

MECHANISM	FY 1999 Actual		FY 2000 Estimate		FY 2001 Estimate	
Research Grants:	No.	Amount	No.	Amount	No.	Amount
Research Projects						
Noncompeting	1,872	$750,759,000	1,995	$740,468,000	2,163	$956,066,000
Administrative supplements	(147)	26,599,000	(97)	27,744,000	(84)	10,019,000
Competing:						
Renewal	223	89,493,000	169	139,317,000	207	86,070,000
New	531	178,303,000	618	264,169,000	432	166,432,000
Supplements	2	225,000	5	368,000	4	280,000
Subtotal, competing	756	268,021,000	792	403,854,000	643	252,782,000
Subtotal, RPGs	2,628	1,045,379,000	2,787	1,172,066,000	2,806	1,218,867,000
SBIR/STTR	102	24,847,000	123	29,923,000	128	31,620,000
Subtotal, RPGs	2,730	1,070,226,000	2,910	1,201,989,000	2,934	1,250,487,000
Research Centers						
Specialized/comprehensive	38	65,491,000	42	73,769,000	42	79,526,000
Clinical research	0	40,942,000	0	41,981,000	0	41,981,000
Biotechnology	0	2,022,000	0	3,151,000	0	3,154,000
Comparative medicine	10	28,074,000	10	32,580,000	10	36,588,000
Research Centers in Minority Institutions	0	6,747,000	0	8,067,000	0	8,534,000
Subtotal, Centers	48	143,276,000	52	159,548,000	52	169,783,000
Other Research						
Research careers	174	19,141,000	189	20,043,000	198	22,108,000
Cancer education	0	137,000	0	150,000	0	160,000
Cooperative clinical research	9	9,550,000	13	21,181,000	13	21,306,000
Biomedical research support	2	1,418,000	3	2,092,000	3	2,092,000
Minority biomedical research support	0	382,000	0	443,000	0	470,000
Other	47	25,745,000	54	29,155,000	55	30,875,000
Subtotal, Other Research	232	56,373,000	259	73,064,000	269	77,011,000
Total Research Grants	3,010	1,269,875,000	3,221	1,434,601,000	3,255	1,497,281,000
Training	FTTPs		FTTPs		FTTPs	
Individual awards	94	3,188,000	97	3,439,000	97	3,513,000
Institutional awards	749	26,305,000	759	28,665,000	759	29,369,000
Total, Training	843	29,493,000	856	32,104,000	856	32,882,000
Research & development contracts	155	188,185,000	186	218,259,000	193	247,316,000
(SBIR/STTR)	(4)	(1,331,000)	(5)	(1,750,000)	(5)	(1,750,000)
Intramural research		189,903,000		206,752,000		214,748,000
Research management and support		60,780,000		64,690,000		67,282,000
Cancer prevention & control		0		0		0
Construction		1,000,000		0		0
Library of Medicine		4,114,000		5,063,000		5,193,000
Office of the Director		43,289,000		44,714,000		46,522,000
Subtotal		1,786,639,000		2,006,183,000		2,111,224,000
Buildings and Facilities		6,100,000		0		0
(Vaccine Facility)		(6,100,000)		(0)		(0)
Total, NIH		1,792,739,000		2,006,183,000		2,111,224,000
(Clinical Trials)		(381,814,000)		(425,700,000)		(447,931,000)

NATIONAL INSTITUTES OF HEALTH

Office of AIDS Research

Budget Authority by Activity
(dollars in thousands)

Research Area	FY 1999 Actual	FY 2000 Estimate	FY 2001 Estimate	Change
Natural History and Epidemiology	$225,986	$252,752	$266,565	$13,813
Etiology and Pathogenesis	556,047	602,925	631,364	28,439
Therapeutics	486,448	514,291	528,120	13,829
Vaccines	181,732	238,711	267,519	28,808
Behavioral and Social Sciences	242,056	290,194	305,577	15,383
Training and Infrastructure	79,424	80,920	83,668	2,748
Information Dissemination	25,729	27,387	28,411	1,024
Total obligations	1,797,422	2,007,180	2,111,224	104,044
Unobligated balance, available start of year	(5,665)	(997)	--	997
Unobligated balance, available end of year	997	--	--	--
Unobligated balance lapsing	(15)	--	--	--
Total, Budget Authority	1,792,739	2,006,183	2,111,224	105,041

NATIONAL INSTITUTES OF HEALTH

Office of AIDS Research

Summary of Changes

2000 Estimated budget authority		$2,006,183,000
2001 Estimated budget authority		2,111,224,000
Net change		105,041,000
	2000 Current Estimate Base	Change from Base
	Budget Authority	Budget Authority
Changes:		
A. Built-in:		
1. Intramural research:		
a. Within grade increase	58,821,000	$864,000
b. Annualization of January 2000 pay increase	58,821,000	732,000
c. January 2001 pay increase	58,821,000	1,428,000
d. One day less pay	58,821,000	(156,000)
e. Payment for centrally furnished services	42,101,000	1,761,000
f. Increased cost of laboratory supplies, materials, and other expenses	109,830,000	2,837,000
Subtotal		7,466,000
2. Research Management and Support:		
a. Within grade increase	32,837,000	493,000
b. Annualization of January 2000 pay increase	32,837,000	453,000
c. January 2001 pay increase	32,837,000	861,000
d. One day less pay	32,837,000	(77,000)
e. Payment for centrally furnished services	8,067,000	338,000
f. Increased cost of laboratory supplies, materials, and other expenses	23,786,000	615,000
Subtotal		2,683,000
Subtotal, Built-in		10,149,000

NATIONAL INSTITUTES OF HEALTH

Office of AIDS Research
Summary of Changes--continued

	2000 Current Estimate Base		Change from Base	
	No.	Amount	No.	Amount
B. Program:				
1. Research projects grants:				
a. Noncompeting	1,995	$768,212,000	168	$197,873,000
b. Competing	792	403,854,000	(149)	(151,072,000)
c. SBIR/STTR	123	29,923,000	5	1,697,000
Total	2,910	1,201,989,000	24	48,498,000
2. Centers	52	159,548,000	0	10,235,000
3. Other research	259	73,064,000	10	3,947,000
4. Research training	856	32,104,000	0	778,000
5. Research and development contracts	186	218,259,000	7	29,057,000
6. Intramural research		206,752,000		530,000
7. Research management and support		64,690,000		(91,000)
8. Office of AIDS Research		44,714,000		1,808,000
9. National Library of Medicine		5,063,000		130,000
10. Buildings and Facilities		--		--
Subtotal, program				94,892,000
Total changes		2,006,183,000		105,041,000

Note: Includes funds to support personnel included in the individual Institutes and Centers of the NIH.

National Institutes of Health

Office of AIDS Research

AIDS Funding by Institute and Center

Institute/Center	FY 1999 Actual	FY 2000 Estimate	FY 2001 Estimate
NCI	$234,653,000	$244,494,000	$255,342,000
NHLBI	64,511,000	65,527,000	67,175,000
NIDCR	17,959,000	20,193,000	21,100,000
NIDDK	17,846,000	21,983,000	22,907,000
NINDS	29,335,000	33,658,000	34,416,000
NIAID	802,658,000	915,484,000	971,047,000
NIGMS	31,850,000	37,128,000	38,696,000
NICHD	75,745,000	89,540,000	94,204,000
NEI	10,351,000	10,890,000	11,176,000
NIEHS	7,023,000	7,541,000	7,678,000
NIA	2,068,000	4,143,000	4,298,000
NIAMS	4,683,000	5,022,000	5,233,000
NIDCD	1,690,000	1,590,000	1,591,000
NIMH	114,105,000	128,697,000	135,294,000
NIDA	188,919,000	218,227,000	229,173,000
NIAAA	16,187,000	19,243,000	20,083,000
NINR	6,229,000	7,497,000	7,810,000
NHGRI	3,989,000	4,188,000	4,313,000
NCRR	95,957,000	105,915,000	111,464,000
NCCAM	1,030,000	1,030,000	1,030,000
FIC	12,448,000	14,416,000	15,479,000
NLM	4,114,000	5,063,000	5,193,000
OD	43,289,000	44,714,000	46,522,000
B&F	6,100,000	0	0
TOTAL	1,792,739,000	2,006,183,000	2,111,224,000

NATIONAL INSTITUTES OF HEALTH

OFFICE OF AIDS RESEARCH

BUDGET AUTHORITY BY OBJECT

	Object Class	FY 2000 Estimate	FY 2001 Estimate	Increase or Decrease
	Personnel Compensation:			
11.1	Full-Time Permanent	54,950,420	59,149,300	$4,198,880
11.3	Other than Full-Time Permanent	10,923,000	11,897,000	974,000
11.5	Other Personnel Compensation	3,004,000	3,248,000	244,000
11.8	Special Personnel Services Payments	6,580,000	7,188,000	608,000
11.9	**Total Personnel Compensation**	**75,457,420**	**81,482,300**	**6,024,880**
12.0	Personnel Benefits	17,582,580	19,026,700	1,444,120
13.0	Benefits for Former Personnel	1,000	2,000	1,000
	Subtotal, Pay Costs	**93,041,000**	**100,511,000**	**7,470,000**
21.0	Travel & Transportation of Persons	4,785,000	4,867,000	82,000
22.0	Transportation of Things	573,000	580,000	7,000
23.1	Rental Payments to GSA	2,926,000	2,995,000	69,000
23.2	Rental Payments to Others	2,658,000	2,739,000	81,000
23.3	Communications, Utilities & Miscellaneous Charges	3,293,000	3,387,000	94,000
24.0	Printing & Reproduction	796,000	813,000	17,000
25.1	Consulting Services	4,114,000	4,285,000	171,000
25.2	Other Services	46,952,000	46,896,000	(56,000)
25.3	Purchase of Goods & Services from Government Accounts	127,715,000	143,653,000	15,938,000
25.4	Operation & Maintenance of Facilities	33,138,000	34,927,000	1,789,000
25.5	Research & Development Contracts	163,749,000	180,744,000	16,995,000
25.6	Medical Care	1,040,000	1,044,000	4,000
25.7	Operation & Maintenance of Equipment	2,068,000	2,075,000	7,000
25.8	Subsistence & Support of Persons	0	0	0
25.0	**Subtotal, Other Contractual Services**	**378,776,000**	**413,624,000**	**34,848,000**
26.0	Supplies & Materials	26,604,000	26,742,000	138,000
31.0	Equipment	14,312,000	15,071,000	759,000
32.0	Land and Structures	0	0	0
33.0	Investments & Loans	0	0	0
41.0	Grants, Subsidies & Contributions	1,464,846,000	1,525,276,000	60,430,000
42.0	Insurance Claims & Indemnities	13,567,000	14,613,000	1,046,000
43.0	Interest & Dividends	6,000	6,000	0
44.0	Refunds	0	0	0
	Subtotal, Non-Pay Costs	**1,913,142,000**	**2,010,713,000**	**97,571,000**
	Total Budget Authority	**2,006,183,000**	**2,111,224,000**	**105,041,000**

Note: Includes funds to support personnel included in the Institutes and Centers of the NIH.

NATIONAL INSTITUTES OF HEALTH

OFFICE OF AIDS RESEARCH

SALARIES AND EXPENSES

	FY 2000 Estimate	FY 2001 Estimate	Change
Personnel Compensation:			
Full-Time Permanent (11.1)	$54,950,420	$59,149,300	$4,198,880
Other Than Full-Time Permanent (11.3)	10,923,000	11,897,000	974,000
Other Personnel Compensation (11.5)	3,004,000	3,248,000	244,000
Special Personnel Services Payments (11.8)	6,580,000	7,188,000	608,000
Total Personnel Compensation (11.9)	**75,457,420**	**81,482,300**	**6,024,880**
Civilian Personnel Benefits (12.0)	17,582,580	19,026,700	1,444,120
Benefits to Former Personnel (13.0)	1,000	2,000	1,000
Subtotal, Pay Costs	**93,041,000**	**100,511,000**	**7,470,000**
Travel (21.0)	4,785,000	4,867,000	82,000
Transportation of Things (22.0)	573,000	580,000	7,000
Rental Payments to Others (23.2)	2,658,000	2,739,000	81,000
Communications, Utilities and Miscellaneous Charges (23.3)	3,293,000	3,387,000	94,000
Printing and Reproduction (24.0)	796,000	813,000	17,000
Other Contractual Services:			
Advisory and Assistance Services (25.1)	4,114,000	4,285,000	171,000
Other Services (25.2)	46,952,000	46,896,000	(56,000)
Purchases from Govt. Accounts (25.3)	38,918,000	39,219,000	301,000
Operation & Maintenance of Facilities (25.4)	6,295,000	6,472,000	177,000
Operation & Maintenance of Equipment (25.7	2,068,000	2,075,000	7,000
Subsistence & Support of Persons (25.8)	0	0	0
Subtotal Other Contractual Services	**98,347,000**	**98,947,000**	**600,000**
Supplies and Materials (26.0)	26,582,000	26,719,000	137,000
Subtotal, Non-Pay Costs	137,034,000	138,052,000	1,018,000
Total, Salaries and Expenses	**230,075,000**	**238,563,000**	**8,488,000**

Note: Includes funds to support personnel included in the Institutes and Centers of the NIH.

NATIONAL INSTITUTES OF HEALTH
Office of AIDS Research

SIGNIFICANT ITEMS IN HOUSE AND SENATE
APPROPRIATIONS COMMITTEE REPORTS

FY 2000 House Appropriations Committee Report Language (H. Rpt. 166-370)

Item

[HIV/AIDS prevention and treatment]-- The Committee encourages Federal HIV/AIDS services and prevention funds be responsive to the demographic trends of the epidemic. (p. 110)

Action taken or to be taken

AIDS in Minority Communities–The changing demographics in the epidemic demand careful consideration in planning the NIH research agenda, since different prevention and intervention strategies must be applied to each subepidemic. In response to that need, this year, a new area of special interest section on Racial and Ethnic Minorities was added to the annual NIH Plan for HIV-Related Research. To advise OAR on the scientific priorities in this critical research area, OAR established a new advisory group, the Ad Hoc Working Group on Minority Research, which includes scientific experts as well as community representatives.

NIH supports a broad array of behavioral intervention studies with specific focus on African American and other minority populations. These studies are characterizing the disease process in drug users, factors influencing disease progression, consequences of multiple co-infections, effectiveness of therapeutic regimens, and impact of health care access and adherence to therapeutic regimens on disease outcomes.

On October 27, 1998, the Administration and the Congressional Black Caucus announced a major initiative to address the disproportionate impact of HIV/AIDS in minority populations. NIH has responded to the initiative with projects to: increase the number of minority investigators conducting behavioral and clinical research; target the links between substance abuse, sexual behaviors and HIV infection; and increase outreach education programs for minority physicians and at-risk populations.

NIH has devoted resources to improve research infrastructure and minority training opportunities, and we will continue to assure the participation of minorities in clinical trials and in natural history, epidemiology, and prevention studies. We are focusing on interventions that address co-occurrence of other STDs, hepatitis, drug abuse, and mental illness, and those that consider the role of culture, family, and other social factors in minority communities.

Women and AIDS–Heterosexual transmission, the primary route of HIV infection worldwide, accounts for an increasing proportion of new infections among women and racial/ethnic minorities in the U.S., and NIH is directing resources toward new interventions that will have the

greatest impact on these groups. For example, NIH places a high priority on studies to develop effective and acceptable female-controlled methods to block HIV transmission, such as topical microbicides.

NIH supports a comprehensive program of research to address the important research issues unique to HIV-infected women. For example, in the area of basic research, NIH supports studies on the characterization of cells susceptible to HIV infection in both the lower and upper reproductive tract and the influence of hormonal modulation on viral infectivity and vaginal immunity. The Women's Interagency HIV Study (WIHS) is a major effort to identify the nature and rate of HIV disease progression in women, characterizing the clinical manifestations of HIV important to women, and assessing the effects of therapeutic regimens. The majority–82 percent–of the women in these studies are women of color. The NCI Special Surveillance Study is defining the incidence and spectrum of the histopathology of cervical cancer in HIV-infected women. NIH also supports a rigorous program of behavioral and social science research aimed at understanding the determinants of HIV risk behavior among women and designing effective interventions to change such behavior.

International Communities–Because HIV has spread rapidly around the globe, without respect to political boundaries, it can only be controlled through a global program of interventions. More than 90 percent of new infections occur in developing countries, where therapeutic interventions are unaffordable and undeliverable. NIH must pursue interventions that can be implemented in these resource- and infrastructure-deprived nations. Our vaccine research efforts underscore the crucial role of NIH in addressing prevention and treatment needs worldwide. In addition, a recent clinical trial demonstrated that nevirapine, an inexpensive drug, could reduce mother-to-child transmission by 50 percent. NIH has established research and training programs in many developing nations. To further these efforts, OAR has established an International AIDS Research Collaborating Committee to bring together all of the Departments of the U.S. government conducting AIDS research and our international partners, including the U.N. Joint Programme on AIDS and the World Bank.

Item

Office of AIDS Research – The OAR develops a comprehensive plan for NIH AIDS-related research activities which is updated annually. The plan is the basis for the President's budget distribution of AIDS-related funds to the Institutes, centers and divisions within NIH. The Committee expects the Director of NIH to use this plan and the budget developed by OAR to guide his decisions on the allocation of AIDS funding among the Institutes. The Director of NIH also should use the full authority of his office to ensure that the ICDs spend their AIDS research dollars in a manner consistent with the plan. In addition, the OAR allocates an emergency AIDS discretionary fund to support research that was not anticipated when budget allocations were made. (p. 111)

Action taken or to be taken

The OAR has allocated all monies for AIDS-related research to the Institutes and Centers in accordance with the scientific priorities and objectives of the NIH FY 2000 Plan for HIV-Related Research. At the end of each fiscal year, the Institutes and Centers report spending for the previous year by the objectives set forth in the Plan. This information is reviewed by the Office of AIDS Research for consistency and adherence to the research priorities contained in the plan.

Item

[NIH Director's transfer authority]--The Committee has included the same general provisions in bill language that was contained in the 1999 appropriations bill. This language permits the Director of OAR, jointly with the Director of NIH, to transfer between ICDs up to three percent of the funding determined by NIH to be related to AIDS research. This authority could be exercised throughout the fiscal year subject to normal reprogramming procedures, and is intended to give NIH flexibility to adjust the AIDS allocations among Institutes if research opportunities and needs should change. The Committee also repeats language from last year's bill making the research funds identified by NIH as being AIDS related available to the OAR account for transfer to the Institutes. This provision permits the flow of funds through the OAR in the spirit of the authorization legislation without requiring the Congress to earmark a specific dollar amount for AIDS research. (p. 111)

Action taken or to be taken

The OAR has allocated all monies for AIDS-related research to the Institutes and Centers of the NIH in accordance with the FY NIH 2000 NIH Plan for HIV-Related Research. The flexibility provided by the transfer authority in managing the NIH portfolio is extremely important. As a result of our rigorous planning process, it has not been necessary to utilize this authority. However, in the event of new scientific discoveries, this authority will allow us to shift resources and act quickly to address scientific needs. The OAR will notify the Committee in the event the 3 percent transfer authority is utilized.

Item

[HIV/AIDS Research Centers]-- The Committee is supportive of the efforts of the NIH to create extramural, multidisciplinary HIV/AIDS Research Centers and understands that there has been substantial scientific benefit from these Centers, particularly in the effort to prevent new HIV infections, the care for people living with HIV disease, and the advancement of basic biomedical research efforts. The Committee encourages NIH to enhance its support for these Centers. (p. 111)

Action taken or to be taken

During the past year, the Director of the Office of AIDS Research and the NIH institutes that co-fund the Centers for AIDS Research (CFAR) Program -- the National Institute of Allergy and

Infectious Diseases (NIAID), the National Institute of Child Health and Human Development (NICHD), the National Cancer Institute (NCI), the National Institute on Mental Health (NIMH), the National Institute on Drug Abuse (NIDA), and the National Heart, Lung, and Blood Institute (NHLBI)–convened a Focus Group of non-government scientists and other experts to conduct a comprehensive and objective review of the CFAR Program. The NIH charge to the Focus Group was to address the role of the CFAR within the NIH AIDS research portfolio, the size of the program (e.g., number of centers and total funding), the criteria to be considered in determining funding levels, the milestones for its evaluation, and to determine what changes may further improve the CFAR program.

Under the chairmanship of Dr. Barney Graham of Vanderbilt University, the Focus Group developed a report with recommendations that was submitted to the Office of AIDS Research Advisory Council and to the Advisory Councils of the relevant NIH Institutes and Centers. The Focus Group Report commended the CFAR program for its overall success and made recommendations for its future development in four major categories: (1) the size and cost, (2) the application and evaluation process, (3) the administration of the program, and (4) the future goals.

The CFAR Steering Committee, comprised of representatives of the OAR and the relevant institutes, prepared an implementation plan to address the recommendations of the report. NIH has already taken a number of steps to implement the recommendations and to enhance support for this important program, including:

- Developed a long-term plan for the program;
- Established a new tier of developmental awards beginning in FY 2001; and
- Simplified and streamlined the administrative and grants management procedures for the program.

In addition, a new program announcement is being prepared for the CFAR program, in which the recommendations focusing on the application and evaluation process will be implemented. This will ensure that the spirit of the report's recommendations will directly affect the future of the overall program.

Item

[HIV/AIDS prevention and treatment]-- The Committee encourages Federal HIV/AIDS services and prevention funds be responsive to the demographic trends of the epidemic. (p. 111)

Action taken or to be taken

Please refer to page 32 of this document for OAR's response to this significant item regarding HIV/AIDS prevention and treatment.

FY 2000 Senate Appropriations Committee Report Language (S. Rpt. 106-166)

Pediatric AIDS Clinical Trials Group (PACTG)-- . . . The Committee urges NIH to support PACTG inclusion in overall future NIH, HIV research agendas and the conduct of protocols for children, youth and women domestically and internationally. The Committee urges NIH to seek input from the Ryan White CARE Act Title IV projects in the development of protocols in order to maximize patient participation. (p. 181)

Action taken or to be taken

The Pediatric AIDS Clinical Trials Group (PACTG) is a nationwide, multicenter network that conducts clinical trials of treatments for HIV infection among infants, adolescents, and pregnant women. These clinical studies include the testing of potential approaches to interrupt the transmission of HIV infection from mother to infant. This network is collaboratively supported by the National Institute of Allergy and Infectious Diseases (NIAID) and the National Institute of Child Health and Human Development. The PACTG has expanded the clinical trials enrollment in both domestic and international sites. Clinical protocols are currently ongoing in several developing and developed nations, including Trinidad, Tobago, Jamaica, Bahamas, Brazil, England, Spain, Italy, and Switzerland. The competitive renewal of the NIAID-supported component of the PACTG is planned for FY 2001.

Pediatric AIDS research, especially prevention and treatment of HIV infection among adolescents, is a high priority for the NIH. This research area is included in all of the scientific areas of the NIH Plan for HIV-Related Research that is annually developed to reflect the state-of-the-science and to ensure that critical scientific opportunities and questions are identified and programs are implemented to address these priorities. In June 1999, NIH convened a Working Group of non-government experts and community participants to review recent epidemiologic data as well as recent therapeutic and prevention research findings and NIH-supported programs with the goal of providing advice to the NIH on future perinatal, pediatric, and adolescent HIV research priorities. The Working Group report, which was released in January 2000, contains recommendations that will have significant impact on the future scientific agenda for NIH-sponsored pediatric HIV research. The Report will be provided to the Office of AIDS Research (OAR) Director and the OAR Advisory Council as well as to the Institutes and Centers so that the recommendations can be implemented through the development of new initiatives and recompetition of existing programs.

The PACTG continues to collaborate closely with the Ryan White CARE Act Title IV sites enrolling HIV-infected individuals in selected PACTG clinical trials. Two recent examples of these collaborations are described here. Eight of these sites have been funded since 1998 to enroll infants born to HIV-infected mothers in a clinical protocol to evaluate the effect of formula feeding versus calorie-enhanced formula on the growth and disease progression of HIV-infected infants. In addition, six Ryan White CARE Act Title IV sites were recently funded to conduct a PACTG protocol in an ongoing prospective evaluation of trends in antiretroviral treatment and

pregnancy outcome of HIV-infected women at these sites. The NIH will continue to work collaboratively with the Ryan White Title IV sites in the development and the conduct of PACTG studies.

NATIONAL INSTITUTES OF HEALTH

Office of AIDS Research

Authorizing Legislation

	PHS Act/ Other Citation	U.S. Code Citation	2000 Amount Authorized	2000 Estimate	2001 Amount Authorized	2001 Budget Estimate
Research and Investigation	Section 301	42§241	Indefinite	---	Indefinite	$2,021,820,000
Office of AIDS Research	Title XXIII Section 2353(d)(1)	42§300cc-40b(d)	a/	---	b/	46,522,000
Discretionary Fund	Title XXIII Section 2356(g)(1)	42§300cc-43(g)	a/	---	b/	10,000,000
National Research Service Awards	Section 487(d)	42§288(d)	a/	---	b/	32,882,000
Total, Budget Authority			---	---		2,111,224,000

a/ Funding provided under Departments of Labor, Health and Human Services, Education, and Related Agencies Appropriations Act, 2000 (P.L. 106-113).

b/ Reauthorizing legislation will be submitted.

NATIONAL INSTITUTES OF HEALTH

Office of AIDS Research

Appropriation History

Fiscal Year	Budget Estimate to Congress 1/	House Allowance	Senate Allowance	Appropriation
1995	$1,379,052,000	$1,337,606,000	$1,337,606,000	$1,335,421,000 2/
1995 Rescission				(1,851,000)
1996	1,407,824,000	3/	1,382,861,000	4/
1997	1,431,908,000	3/	1,460,312,000	4/
1998	1,540,765,000	3/	5/	4/
1999	1,728,099,000 6/	3/	5/	4/
2000	1,833,826,000	3/	5/	4/
2001	2,111,224,000			

1/ Includes all amounts associated with the National Institutes of Health AIDS Research Program.

2/ Excludes procurement reform, rent, and salary and expense reductions of $2,185,000.

3/ The House did not provide separate funding for HIV/AIDS activities. The funds to support these activities are included in the appropriations of the Institutes and Centers.

4/ The Conferees did not provide separate funding for HIV/AIDS activities. The funds to support these activities are included in the appropriations of the Institutes and Centers.

5/ The Senate did not provide separate funding for HIV/AIDS activities. The funds to support these activities are included in the appropriations of the Institutes and Centers.

6/ Reflects a decrease of $2,697,000 for the budget amendment for bioterrorism.